PATENT

UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 97-022-F3)

IN THE APPLICATION OF:			
R. Terry Dunlay, *et al.*			
Serial No.	**09/718,770**	Examiner:	**Smith, Carolyn L.**
Filed:	**November 22, 2000**	Group Art Unit:	**1631**
Title	**A System for Cell-Based Screening**	Confirmation No.:	**5398**

APPELLANTS' BRIEF IN SUPPORT OF THE APPEAL TO THE BOARD OF PATENT APPEAL AND INTERFERENCES

Dear Sir:

This Appeal Brief is submitted pursuant 37 C.F.R. 41.37, within five months from the February 15, 2007 mailing of the Notice of Appeal and is accompanied by a request for an extension of time for three months and the required fee of $1020.00. If additional fees are due the Commissioner is authorized to charge our deposit account number 13-1249.

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I. Real Party in Interest

The real party in interest is Cellomics, Inc., the assignee of record, which is a subsidiary of Thermo Fisher Scientific.

II. Related Appeals and Interferences

An Appeal Brief was filed on August 12, 2003 along with a Notice of Appeal in related U.S. Patent Application Serial No. 09/624131, filed July 21, 2000 now U.S. Patent No. 7,160,687, issued January 9, 2007. A Request for Continued Examination was subsequently filed on September 27, 2005 before a decision was rendered by the Board of Patent Appeals and Interferences.

III. Status of Claims

Claims 13-18 and 23-25 are pending in this application and stand rejected. These claims were finally rejected in the Office Action mailed November 6, 2006, and Applicants received an Advisory Action, mailed January 30, 2007. A Notice of Appeal was mailed via Express Mail with a certificate of mailing on February 15, 2007. This Appeal Brief is being filed within five months of the filing of the Notice of Appeal and is accompanied by the proper request for an extension of time for three months accompanied by the required fee.

A clean set of the pending claims is attached in the Claims Appendix beginning at page 17.

IV. Status of Amendments

No claims have been amended or canceled in the instant brief.

V. Summary of Claimed Subject Matter

The invention relates to a method for acquiring, storing and retrieving cell screening data on a computer system. The invention involves collecting and storing subcellular image data from cells in wells on a plate. The subcellular data is then used to generate feature data; the subcellular image data and feature data are used to generate well summary data, and the well summary data is used to generate plate summary data;

with the data stored in a computer system database from where it can be retrieved.

VI. Grounds of Rejection to be Reviewed on Appeal

1. Whether claims 13-18 and 23-25 are unpatenable under 35 U.S.C. § 102(e)(2) over Patent No. 5,961,923, (hereinafter, "Nova").

VII. Argument

There is only one remaining rejection of claims 13-18 and 23-25 under 35 U.S.C. § 102(e)(2) as anticipated over Nova.

Applicants respectfully assert that the Patent Office's rejection does not meet the statutory standard required for an anticipation rejection. The reasons supporting patentability are set forth below.

A. The Office Erred in Rejecting Claims 13-18 and 23-25 as being Anticipated over Nova *et al.*

Claims 13-18 and 23-25 stand rejected as anticipated over Nova. For the following reasons, the Applicants respectfully traverse.

i. The cited reference does not teach or disclose all of the claim limitations

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference" *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). (MPEP §2131) "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." (MPEP Section 2112, IV)

Presently pending claim 13 recites as follows:

> A method for acquisition, storage, and retrieval of cell screening data on a computer system, comprising the steps of :
>
> a) providing a plate containing wells, wherein the wells comprise cells;
>
> b) storing input parameters used for screening of the plate in a

computer system database;

c) repeating steps (i)-(ix) for a desired number of wells:

i) selecting an individual well on the plate,

ii) collecting **subcellular image data from the cells** in the well,

iii) storing the **subcellular image data** in the computer system database,

iv) collecting **feature data** from the **subcellular image data**,

v) storing the feature data in the computer system database,

vi) calculating well summary data using the **subcellular image data** and the feature data collected from the well;

vii) storing the well summary data in the computer system database;

viii) calculating plate summary data using the well summary data from the computer system database; and

ix) storing the plate summary data in the computer system database;

wherein the subcellular image data, the feature data, the well summary data, and the plate summary data can be retrieved from the computer system database. (emphasis added)

As argued by Applicants in previous responses, Nova does not teach or disclose collecting **subcellular image data from cells** in the wells (as required in pending claim 13(c)(ii)), nor, as a result, any further steps involving subcellular image data: (ie:

- collecting feature data from the subcellular image data (c)(ii);
- storing subcellular image data (c) (iii);
- calculating well summary data from the subcellular image data and feature data (c)(vi); and
- calculating plate summary data from the well summary data (c)(vii)),

as recited in the presently pending claims.

The Patent Office asserts that "sub-cellular image data" is defined as "anything involving subcellular and image data (i.e. data from labeled proteins detected using a photodetector...)" and that Nova has taught collecting, storing, and retrieving subcellular image data according to this definition of subcellular image data. However, as argued by Applicants in previous responses, the Patent Office has provided no basis for this definition of subcellular image data, except for its own assertion, and has failed to note the entirety of the instant claims, which state "collecting **subcellular image data from**

the cells..." It would thus be clear to one with skill in the art that the instant claims recite collecting image data from subcellular components **within cells.**

The Patent Office has cited a number of passages in Nova as support for its assertion that Nova teaches collecting subcellular image data. Applicants respectfully traverse. The Patent Office has misinterpreted the teaching of Nova in general and particularly with respect to the instant claim limitation of claim 13 which recites "collecting subcellular image data from the cells." The passages cited by the Patent Office in support of its assertion that Nova teaches generating subcellular image data, and the corresponding Patent Office arguments are detailed in the Table below. However particular passages cited by the Patent Office clearly demonstrate the inadequacy of the Patent Office's arguments. For example, the abstract of Nova, cited by the Patent Office as a key component of its argument that Nova teaches generating subcellular image data, states the following:

> "**Combinations**, called **matrices with memories**, of **matrix materials** that are encoded with an optically readable code are provided. The matrix materials are those that **are used in as supports in solid phase chemical and biochemical syntheses, immunoassays and hybridization reactions.** The matrix materials **may additionally include** fluophors or other luminescent moieties to produce luminescing matrices with memories. The memories include electronic and optical storage media and also include optical memories, such as bar codes and other machine-readable codes. By virtue of this **combination**, **molecules and biological particles**, such as phage and viral particles and cells, that **are in proximity or in physical contact with the matrix combination** can be labeled by programming the memory with identifying information and can be identified by retrieving the stored information. **Combinations** of **matrix materials**, memories, and **linked molecules and biological materials** are also provided. The combinations have a multiplicity of applications, including **combinatorial chemistry, isolation and purification of target macromolecules**,..." (emphasis added)

This passage defines "matrices with memories" as combinations of **matrix materials** that are encoded with an optically readable code. The matrix materials are defined as materials that are "used as **supports in solid phase chemical and biochemical synthesis, immunoassays, and hybridization reactions."** Thus, matrix materials are used as **supports** in **solid phase** assays as described. It is well known to those of skill in the art that solid phase supports, such as plates, beads, or columns (see, for example, col. 90, lines 25-31; col. 93, line 65-col. 94, line 9; col. 102, lines 21-29 for

Nova examples of matrix materials) are **not located within cells.** The abstract goes on to recite that "molecules and biological particles, such as phage and viral particles and cells, that **are in proximity or in physical contact with the matrix combination can be labeled**..." Thus, Nova teaches that, in order to be labeled, the molecules or biological particles must be **in proximity to or physically contacted with the matrix combination.** As noted above, it is well known to those of skill in the art that solid supports (ie: the matrices) are not located within cells. Thus, it would be clear to those of skill in the art that any molecules and biological particles in proximity to or in physical contact with the matrix combination would not be located within a cell, and thus that any fluorescence image data generated from such molecules or biological particles in proximity to or physically contacted with the matrix combination would **not be subcellular image data.**

In summary, the Nova abstract clearly teaches that **none** of the "matrix materials," the "matrix combinations," the "molecules," the "biological particles," the "fluorophores," or the "luminescent moieties" are located inside cells. Thus, by definition, **no subcellular image data can be generated** based on the teachings of the Nova abstract.

The Patent Office further cites Nova, column 7, lines 6-32 as a key component of its argument that Nova teaches generating subcellular image data. The Patent Office asserts in the advisory action that this section teaches "tagging molecules such as antigens, antibodies, ligands, proteins and nucleic acids." As noted in the table below, the passage cited by the Patent Office recites the following

> "...tagging molecules, such as antigens, antibodies, ligands, proteins and nucleic acids, and biological particles, such as phage and viral particles and cells, that **are associated with, such as in proximity to or in physical contact with the matrix combination**." (emphasis added)

This section is completely consistent with Applicants' discussion of the abstract above: Nova teaches that, in order to be labeled, the molecules or biological particles must be **associated with, such as in proximity to or physically contacted with the matrix combination.** As noted above, it is well known to those of skill in the art that solid supports (ie: the matrices) are not located within cells. Thus, it would be clear to those of skill in the art that any antigens, antibodies, ligands, proteins and nucleic acids,

and biological particles, such as phage and viral particles and cells associated with the matrices, such as in proximity to or in physical contact with the matrix combination would not be located within a cell, and thus that any fluorescence image data generated from such molecules or biological particles in proximity to or physically contacted with the matrix combination would **not be subcellular image data.** This is supported by examples from Nova (col. 90, lines 25-31 (plates coated with antibodies); col. 93, line 65-col. 94, line 9 (receptor coated beads) ; col. 102, lines 21-29 (antigens or antibodies bound to a solid support), each of which teaches the use of a biological molecule bound to a solid support.

In the Advisory Action, the Patent Office asserted that the Applicant argued in its previous response that "antigens, antibodies, ligands and nucleic acids' are not located in a cell and are thus not sub-cellular." This is a mischaracterization of the Applicants' arguments in the previous response. In fact, the argument made in the previous response was that antigens, antibodies, ligands and nucleic acids are not **necessarily** contained within a cell; they can be **isolated away from cells**, such as for use in solid phase chemical and biochemical synthesis, immunoassays, and hybridization reactions (ie: as used by Nova in association with solid supports).

Finally the Patent Office asserts that Nova "Disclose optical memory devices (OMD) and image acquisition from a camera that can be displayed to the system monitor including edges and peak signals, as well as determining the average intensity of each cell (col. 9, line 18; col. 51, line 61 to col. 52, line 9 and lines 27-60) which represents collecting image data, intensity analysis, and feature data of cells." These passages make no reference to subcellular images of cells. Instead, the relevant section from Nova states as follows:

"Having determined the orientation and spacing of the symbol, **the symbol is broken into sections [step 1011], or cells**, and the average intensity for each cell is determined [step 1012] to permit calculation of the threshold [step 1013] for distinguishing a dark from a light area **of the code**." (emphasis added)

As is clear, this passage from Nova refers to **"cells" to describe discrete sections of a symbol**. Furthermore, column 52 lines 27-60 (and corresponding Figure 31) involve determining edges and peaks for the ***symbol*** (see column 52 lines 45, 48, and 57). As

noted in column 22 line 65-67, **symbology** refers to **the code, such as a bar code, that is engraved or imprinted on the optical memory device**. This is clear from the quote above, which states that the average intensity for each cell is determined to "permit calculation of the threshold...for distinguishing a dark from a light area **of the code."** Thus, it is clear that, as used by Nova in the section cited by the Patent Office, "cells" refers to sections of the bar code (or other code) engraved or imprinted on the optical memory device. Therefore, any average intensity determined from each cell as taught in this section of Nova has nothing whatsoever to do with subcellular image data as recited in the currently pending claims.

The following Table outlines the Nova passages cited with particularity by the Patent Office as well as the Patent Office's corresponding argument and Applicants' response which were previously found unpersuasive. As detailed above and as previously argued, none of the cited passages teach the instant claim limitation of claim 13 of "collecting **subcellular image data from the cells,**" nor any of the other limitations of claim 13 involving image data or its analysis.

Nova-Examiner Cited Sections (emphasis added)	**Corresponding Examiner's Argument**	**Applicant's Response**
Column 88, lines 16-34 "The software then uses the scanner to read a tag and receive its encoded information. Using the user-entered compound names stored in the library's data base, the software translates the encoded information into the names of the chemical building blocks. The software can also display compounds graphically, using the graphical information specified by the user. The software calculates the molecular weight of compounds from the data provided for the pharmacophore and building blocks. The software facilitates the recording of progress through the above process. The software generates displays and reports which illustrate this and all of the above planning, design, compound data, and graphical representations of compounds. An example of the software [to be commercialized under the name Synthesis Manager] and use thereof is set forth in Appendix 3 and in the Examples, below. Once armed with the instant disclosure, other such	"Disclose software reading one tag and encoded information including graphical displays, reports including progress"	This cited section discusses methods for displaying and storing compound structure, compound names, and compound characteristics; there is no teaching or disclosure to collect **subcellular** image data from cells, as recited in the pending claim.

software can be developed by one skilled in that art."		
Column 88, lines 55-62 "When the chemical synthesis is complete, compounds are cleaved from the microreactors and archived. The software provides archival capability for either individual vials or a 96-well format or will be adapted for other formats. Specific columns, rows, or individual well scan be protected to accommodate the need for standards and controls in virtually any screening format. The software provides several utilities that permit one tag to be read at any time, display the corresponding building block names and structures, and the current synthesis status of that compound. It is also possible to search for a specific compound or compounds that contain certain building blocks. For compounds that have already been archived, the archive location [i.e., microplate group name, number, and well] will be displayed."	Teach "searching for specific compounds with certain building blocks (feature data) including those already archived by displaying structure, archive location, microplate group name number and well."	This cited section discusses use for chemical synthesis (and continues discussion on compound naming and characterization) there is no teaching or disclosure to collect **subcellular** image data from cells, as recited in the pending claim.
Abstract "**Combinations**, called matrices with memories, of **matrix materials** that are encoded with an optically readable code are provided. The matrix materials are those that are used in as supports in **solid phase** chemical and biochemical syntheses, immunoassays and hybridization reactions. The matrix materials may additionally include fluophors or other luminescent moieties to produce luminescing matrices with **memories**. The memories include electronic and optical storage media and also include optical memories, such **as bar codes** and other machine-readable codes. By virtue of this combination, molecules and biological particles, such as phage and viral particles and cells, that **are in proximity or in physical contact with the matrix combination** can be labeled by programming the memory with identifying information and can be identified by retrieving the stored information. Combinations of matrix materials, memories, and linked molecules and biological materials are also provided. The combinations have a multiplicity of applications, including combinatorial chemistry, isolation and purification of target macromolecules, capture and detection of macromolecules for analytical purposes, selective removal of contaminants, enzymatic catalysis, cell sorting, drug delivery,	Teach "using fluorophores or other luminescent moieties, labeling molecules and biological particles, tagging molecules"	As discussed above, this passage defines "matrices with memories" as combinations of **matrix materials** that are encoded with an optically readable code. The matrix materials are defined as materials that **are** "used as **supports in solid phase chemical and biochemical synthesis, immunoassays, and hybridization reactions."** It is well known to those of skill in the art that solid phase supports are **not located within cells.** The abstract goes on to recite that the "molecules and biological particles, such as phage and viral particles and cells, that **are in proximity or in physical contact with the matrix combination can be labeled**..." Thus, in order to be labeled, the molecules or biological particles must be **in proximity to or physically**

chemical modification and other uses. Methods for tagging molecules, biological particles and matrix support materials, immunoassays, receptor binding assays, scintillation proximity assays, non-radioactive proximity assays, and other methods are also provided."		**contacted with the matrix combination.** Since solid supports (ie: the matrices) are not located within cells, any molecules and biological particles in proximity to or in physical contact with the matrix combination would not be located within a cell, and thus any fluorescence image data generated from such molecules or biological particles in proximity to or physically contacted with the matrix combination would **not be subcellular image data.**
Column 4, lines 58-67 "Analyses of biological interactions and chemical reactions, however, require the use of labels or tags to track and identify the results of such analyses. Typically biological reactions, such as **binding, catalytic, hybridization and signaling reactions**, are monitored by labels, such as radioactive, fluorescent, photoabsorptive, luminescent and other such labels, or by direct or indirect enzyme labels. Chemical reactions are also monitored by direct or indirect means, such as by linking the reactions to a second reaction in which a colored, fluorescent, chemiluminescent or other such product results. These analytical methods, however, are often time consuming, tedious and, when practiced in vivo, invasive. In addition, each reaction is typically measured individually, in a separate assay. There is, thus, a need to develop alternative and convenient methods for tracking and identifying analytes in biological interactions and the reactants and products of chemical reactions."	Teach "tagging molecules such as antigens, antibodies, ligands, proteins, and nucleic acids and tagging by imprinting the matrix with identifying information"	This cited section discusses the need for alternative methods to study various types of reactions with the use of labels; this section provides no teaching whatsoever about how Nova will solve the problem, and there clearly is no teaching or disclosure to collect **subcellular** image data from cells, as recited in the pending claim.
Column 7, lines 6-32 "By virtue of the **memory with matrix combination**, molecules, such as antigens, antibodies, ligands, proteins and nucleic acids, and biological particles, such as phage and viral particles and cells, that **are associated with, such as in proximity to or in physical contact with the matrix combination** or linked via information stored in a remote computer, can be electromagnetically tagged by programming the memory with data corresponding to identifying information or can be tagged by imprinting the	Teach "tagging molecules such as antigens, antibodies, ligands, proteins, and nucleic acids and tagging by imprinting the matrix with identifying	In order to be labeled, the molecules or biological particles must be **associated with, such as in proximity to or physically contacted with the matrix combination.** As noted above, it is well known to those of skill in the art that solid supports (ie: the matrices) are not located within cells. Thus, it would be clear to those of

matrix with identifying information." Programming and reading the **memory** is effected remotely, preferably using electromagnetic radiation, particularly radio frequency [RF] or radar, microwave, or microwave or energies between RF and microwave, or by reading the imprinted information. Optical memories, either bar coded information or optically encoded memories, such as memories that rely on changes in chemical or physical properties of particular molecules are contemplated herein. Memories may also be remote from the matrix, such as instances in which the memory device is precoded with a mark or identifier or the matrix is encoded with a bar code. The identity [i.e., the mark or code] of each device is written to a memory, which may be a computer or a piece of paper or any recording device, and information associated with each matrix is stored in the remote memory and linked to or associated with the code or other identifier.	information, using optical memories that rely on changes in chemical or physical properties of molecules and storing information associated with each matrix including reaction detection."	skill in the art that any antigens, antibodies, ligands, proteins and nucleic acids, and biological particles, such as phage and viral particles and cells associated with the matrices, such as in proximity to or in physical contact with the matrix combination would not be located within a cell, and thus that any fluorescence image data generated from such molecules or biological particles in proximity to or physically contacted with the matrix combination would **not be subcellular image data.**
Column 7, lines 57-67 "The molecules and biological particles that are **associated with the matrix combination**, such as in proximity to or in physical contact or with the matrix combination, can be identified and the results of the assays determined by retrieving the stored data points from the memories. Querying the memory will identify associated molecules or biological particles that have reacted."	Teach "using optical memories that rely on changes in chemical or physical properties of molecules and storing information associated with each matrix including reaction detection"	Nova again makes it clear that his methods involve the use of solid supports (ie: matrices), and any biological molecules or particles must be associated with the solid supports (and therefore they are not subcellular). There is no teaching or disclosure to collect **subcellular** image data from cells, as recited in the pending claim.
Column 10, lines 6-23 "The data storage device or memory can also be programmed by virtue of a **reaction in proximity to or in the vicinity of the matrix with memory.** In particular, the recording devices include memories and also additional components that detect occurrence of external events or to monitor the status of external parameters, such as EM emissions, changes in temperature or pH, ion concentrations and other such solution parameters. For example, recording devices include memories and also	Teach "a photodetector and recording devices to detect fluorescent occurrence or other optical emission"	This section again refers to the need of the methods for using solid supports; there is absolutely no teaching or disclosure to collect **subcellular** image data from cells, as recited in the pending claim.

include a photodectector can detect the occurrence of fluorescence or other optical emission. Coupling this emission with an amplifier and providing a voltage to permit data storage in the matrix with memory during the reaction by way of, for example an RF signal transmitted to and received by an antenna/rectifier combination within the data storage device or providing voltage sufficient to write to memory from a battery [see, e.g., U.S. Pat. No. U.S. Pat. No. 5,350,645 and U.S. Pat. No. 5,089,877], permits occurrence of the emission to be recorded in the memory."		
Column 8, lines 60-67 "The plates may also include a bar code, particularly the two-dimensional optical bar code provided herein on the base of each well or elsewhere. The two-dimensional bar code or other such code is particularly suited for application to each well in a microplate, such as a microtiter plate, that contain 96, 384, 1536 or higher density formats. The bar code may also be used in combination with modules that are..."	Teach "using bar codes associated with each well in a microtiter plate"	This section discusses bar codes; there is absolutely no teaching or disclosure to collect **subcellular** image data from cells, as recited in the pending claim.
Column 9, lines 18 "The resulting combinations are called luminescing memories with matrices."	"Disclose optical memory devices (OMD) and image acquisition from a camera that can be displayed to the system monitor including edges and peak signals as well as determining the average intensity of each cell"	This term is defined as noted in the arguments above, and clearly requires the use of solid supports, which are not subcellular. Thus, the section provides absolutely is no teaching or disclosure to collect **subcellular** image data from cells, as recited in the pending claim.
Column 51, lines 61-Column 52, line 9 "In the exemplary embodiment illustrated in FIG. 24, the CCD detector 344 comprises an array of discrete devices, each of which is a "pixel", capable of storing charge impinging upon it representative of reflected light from the write surface, then reading out the charge as a serial analog waveform. A typical CCD array for bar code scanning has 2048 pixels, however, CCD arrays of other dimensions may be used. In the preferred embodiment, a CCD array of 640.times.480 pixels is used. Using the CCD array, a "snap shot" of the OMD surface is created using known image or frame grabbing	"Disclose optical memory devices (OMD) and image acquisition from a camera that can be displayed to the system monitor including edges and peak signals as well as determining the average intensity of each	This section says absolutely nothing about cells, but instead discuses standard pixel reading. There is absolutely no teaching or disclosure to collect **subcellular** image data from cells, as recited in the pending claim.

techniques, and an analog electrical representative of the snap shot is conducted to the signal processing function 348 within the system controller, which includes an analog-to-digital converter, to convert the signal into an output of the data written on the OMD."	cell"	
Column 52, lines 27-60 "Processing of the image grabbed by the image detector is a significant aspect of the system in that it provides the flexibility to manipulate the image to enhance readability. The steps of the exemplary image processor are provided in the flow diagram of FIG. 31, and the image signal generated by the detector is checked for completeness, validity and orientation, among other things. As discussed above, if systems where physical orientation and positioning of the OMD is not assured by the handling hardware, one aspect of the image processing software is to determine skew or rotation of the image as seen by the detector. " "The following steps are provided in detail in the system processor's software, the code for which is provided as a Microfiche Appendix I, and a portion of which is depicted in the flow diagram of FIG. 31. [Note that the actual image obtained from the camera can be displayed on a system monitor as it is being modified to permit decoding.] First, after obtaining the image from the camera [step 1001], in steps 1002 and 1003, the edges of the symbol in the vertical direction are identified, looking for the highest peak signal to provide a reference, then the horizontal edges are found [step 1004]. Knowing the boundaries of the symbol, the reasonable spacing is determined [step 1005] to correct for missing or extra vertical edges using a neural network approach. Based on the reasonable spacing, it is determined if the length of the vertical edge is appropriate [step 1006]; if not, adjustments are made by adding or removing edges [step 1007]. A similar procedure is used for the horizontal edges [steps 1008-1010], allowing skew to be determined. Having determined the orientation and spacing of the symbol, **the symbol is broken into sections [step 1011], or cells**, and the average intensity for each cell is determined [step 1012] to permit calculation of the threshold [step 1013] for distinguishing a dark from a light area **of the code."**	"Disclose optical memory devices (OMD) and image acquisition from a camera that can be displayed to the system monitor including edges and peak signals as well as determining the average intensity of each cell"	As discussed above, Nova refers to **"cells" to describe discrete sections of a symbol**. This section involves determining edges and peaks for the ***symbol*** (see column 52 lines 45, 48, and 57). As noted in column 22 line 65-67, **symbology** refers to **the code, such as a bar code, that is engraved or imprinted on the optical memory device**. This is clear from the highlighted, which states that the average intensity for each cell to "permit calculation of the threshold...for distinguishing a dark from a light area **of the code."** Thus, it is clear that, as used by Nova in the section cited by the Patent Office, "cells" refers to sections of the bar code (or other code) engraved or imprinted on the optical memory device. Therefore, any average intensity determined from each cell as taught in this section of Nova has nothing whatsoever to do with subcellular image data as recited in the currently pending claims.

Thus, it is clear from the arguments above and the cited passages that Nova is not

a proper anticipatory reference, either expressly or inherently. As detailed above, Nova provides absolutely no express teaching of generating subcellular images from cells, nor then of using the subcellular image data to collect feature data, nor of then using the subcellular image data and the feature data to calculate well summary data, nor then using the well summary data (which is calculated from the feature and subcellular image data) to calculate plate data. Nor can it plausibly be argued that Nova inherently anticipates these limitations of claim 13. Inherency requires that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill, and may not be established by probabilities or possibilities. "The mere fact that a certain thing may result from a given set of circumstances is not sufficient." Given that Nova provides absolutely no teaching or disclosure of generating **any** subcellular image data, there is not even a possibility that the missing descriptive matter (collecting subcellular images from cells, nor then of using the subcellular image data to collect feature data, nor of then using the subcellular image data and the feature data to calculate well summary data, nor then using the well summary data (which is calculated from the feature and subcellular image data) to calculate plate data) is necessarily present in Nova.

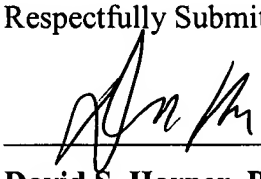
Thus, the Nova reference clearly is not a proper anticipatory reference for claim 13, nor for any of the claims 14-18 and 23-25 which are dependent on claim 13 and which recite further limitations.

B. Conclusion

In summary, the presently claimed methods cannot be anticipated by Nova because Nova does not teach all the elements of the presently pending claims. Nova provides no express or inherent disclosure regarding "collecting subcellular image data from the cells" or other limitations that require use of the collected subcellular image data. Accordingly, the Applicants respectfully submit that this rejection is improper.

Date: 6/26/07

Respectfully Submitted,



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VIII. CLAIMS APPENDIX

1. (Canceled)

2. (Canceled)

3. (Canceled)

4. (Canceled)

5. (Canceled)

6. (Canceled)

7. (Canceled)

8. (Canceled)

9. (Canceled)

10. (Canceled)

11. (Canceled)

12. (Canceled)

13. (Previously presented) A method for acquisition, storage, and retrieval of cell screening data on a computer system, comprising the steps of :

a) providing a plate containing wells, wherein the wells comprise cells;

b) storing input parameters used for screening of the plate in a computer system database;

c) repeating steps (i)-(ix) for a desired number of wells:

i) selecting an individual well on the plate,

ii) collecting subcellular image data from the cells in the well,

iii) storing the subcellular image data in the computer system database,

iv) collecting feature data from the subcellular image data,

v) storing the feature data in the computer system database,

vi) calculating well summary data using the subcellular image data and the feature data collected from the well;

vii) storing the well summary data in the computer system database;

viii) calculating plate summary data using the well summary data from the computer system database; and

ix) storing the plate summary data in the computer system database;

wherein the subcellular image data, the feature data, the well summary data, and the plate summary data can be retrieved from the computer system database.

14. (Previously presented) A computer readable medium having stored therein instructions for causing a computer to execute the method of Claim 13.

15. (Previously presented) The method of Claim 13 wherein the wells include cells treated with a test compound.

16. (Previously presented) The method of Claim 13 wherein the plate comprises a microplate.

17. (Previously presented) The method of Claim 13 wherein the computer system database includes microplate data.

18. (Previously presented) The method of Claim 13 wherein the computer system database includes photographic subcellular image data.

19. (Canceled)

20. (Canceled)

21. (Canceled)

22. (Canceled)

23. (Previously presented) The method of claim 13 wherein the input parameters used for screening of the plate include parameters for one or more of the following: identifying nuclei; identifying cytoplasm; identifying different fluorescent reagents; cell selection settings, number of cells to be analyzed per well, and range of

size, shape, and intensity of cells to be analyzed.

24. (Previously presented) The method of claim 13 wherein the feature data include one or more of: size, shape, intensity, location, area, perimeter squared area, height width ratio, total fluorescence intensity, and average fluorescence intensity.

25. (Previously presented) The method of claim 24 wherein the step of collecting well summary data includes calculating one or more of: size, shape, intensity, location, area, perimeter squared area, height width ratio, total fluorescence intensity, and average fluorescence intensity.

IX. EVIDENCE APPENDIX

None.

X. RELATED PROCEEDINGS APPENDIX

None.